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71 Applicant: **THE WELLCOME FOUNDATION LIMITED,**
183-183 Euston Road, London NW1 2BP (GB)
Applicant: **COOPERS ANIMAL HEALTH LIMITED,**
Berkhamsted Hill, Berkhamsted Hertfordshire (GB)

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72 Inventor: **Baker, Rodney Cyril The Wellcome Research**
Lab., Berkhamsted Hill, Berkhamsted Hertfordshire
(GB)

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74 Representative: **Rollins, Anthony John et al, Group**
Patents & Agreements The Wellcome Research
Laboratories Langley Court, Beckenham Kent BR3 3BS
(GB)

54 **Pharmaceutical composition comprising a medicament and a water-swellable polymer.**

57 **Pharmaceutical compositions for release of a biologically active substance into a desired environment, comprising a biologically active substance, a water swellable polymer material and optionally one or more accessory ingredients, characterised in that the water-swellable polymer material constitutes no more than 7% by weight of the said composition. The compositions are particularly useful for oral administration to the rumen of an animal.**

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COMPOSITIONS

The present invention relates to novel compositions and unit dose forms for release of biologically active substances into desired environments.

It has been known in the field of human medicine to provide pharmaceutical compositions for release of drug over a prolonged period by incorporating a water swellable polymer, such as a cellulose ether, therein. In the stomach, the polymer is believed to form a gel layer over the exterior surface of the pharmaceutical dose unit (for example a tablet) so that the drug then diffuses through this layer. Previously, it has been found that generally, the more polymer in the composition, the slower is the effective rate of drug release. For this reason, the overall polymer content of such compositions has tended to be a substantial porportion by weight of the total.

British Patent No 1,330,829 and United States Patent No 3,507,952 disclose sustained release dosage forms for veterinary use in which the sustained release pattern is achieved by the inclusion of a certain proportion of a lubricant. US Patent No 3,773,921 describes sustained release dosage forms for oral administration to ruminant animals, which comprise a therapeutically active sulfa compound, dibasic calcium phosphate, a binder and a lubricant. These patent specifications however make no reference to the use of water swellable polymers such as cellulose ethers.

The present applicants have now found that in compositions for oral administration to the rumen of an animal, or for other purposes in which the composition is exposed to like conditions, it is advantageous to include a water swellable polymer. This is not necessarily for the purpose of providing slow release but can be for other reasons, such as inhibiting disintegration of the dose unit prior to use. This is particularly the case when the dose unit is in the form of a bolus of compressed powder or granules. The applicants have surprisingly further found that it is advantageous for the total percentage polymer content to be less than that in previously known compositions, particularly if a slow r l as pr fil is desired. The applicants believe that in such circumstances, the rate of

drug release may actually decrease (i. . the duration of release is prolonged) with decreasing polymer content, which is the opposite to what has been observed with the prior compositions referred to above.

Thus, one aspect of the present invention provides a pharmaceutical composition for release of a biologically active substance into a desired environment, comprising said biologically active substance, water swellable polymer material and optionally, one or more accessory ingredients, characterised in that the water swellable polymer material constitutes no more than 7% by weight of the said composition. Preferably, the water swellable polymer material constitutes no more than 5% by weight of the said composition.

In some forms of the invention, the lower weight limit of the water swellable polymer material content is 0.01% or less, preferably 0.1%.

A pharmaceutical composition according to the present invention may be formulated for use in human or veterinary medicine. Such formulations may be presented for example in unit dose form.

A unit dose form according to the present invention may be for example a pharmaceutical unit dose for oral administration to a human or animal such as a bolus, tablet, cachet or lozenge, or it may be a dosage form adapted for use in aquatic environments. In the present invention, dosage forms adapted for veterinary use are preferred.

Especially preferred dosage forms for administration to ruminant animals (e.g. cattle and sheep) are boluses wherein the ingredients are present in the form of compressed powders or granules. To inhibit regurgitation of an intra-ruminal bolus, the bolus should be provided with retention means, for example a geometric feature such as wings (for example as described in UK Patent Specification No: 2 020 181). Alternatively, the retention means may provide overall sufficient density to prevent regurgitation. This may be a weighted metal tube surrounding the exterior of the bolus, such as described in UK Patent Specification No: 1 603 970, a discrete weight such as described in European Patent Specification N : EP 0 164 927 A2 or a densification ingredient mixed with the composition (i.e. as the or one of

said accessory ingredients). A favourable material for this purpose is iron powder. Others include iron filings, other dense metals such as tungsten and dense inorganic compounds, for example barium sulphate, calcium sulphate and calcium phosphate.

Pharmaceutical compositions according to the present invention intended for human therapeutic use may contain one or more pharmacologically active agents such as antibiotics, analgesics, sedatives and the like.

Biologically active substances which may be administered to animals in a pharmaceutical composition according to the present invention include pharmacologically active agents such as anti-infectives, eg. antibacterials and anthelmintics; animal growth promoters; and animal nutrients. Other biologically active substances which may be administered to animals include insecticides and larvicides. In general the biologically active substance may be any of those described in European Patent Specification No. 164 927.

Preferred pharmacological agents for veterinary use include anti-infective agents such as anthelmintics and antibacterials.

Preferred antibacterials include sulphonamides and salts thereof (e.g. sulfanilamide, sulfadiazine, sulfamethisazole, sulfapyridine, sulfathiazole, sulfamerazine, sulfamethazine, sulfisoxazole, sulformethoxine,

2-(p-aminobenzene)-sulfonamide-3-methoxypyrazine (Kelfizina), sulfonyldianiline, mafenide, 5-sulfanilamido-2,4-dimethylpyrimidine, 4-(N'-acetylsulfanilamide)-5,6-dimethoxypyrimidine, 3-sulfanilamido-4,5-dimethylisoxazole, 4-sulfanilamido-5-methoxy-6-decyloxy pyrimidinesulfamonomethoxine, 4-p-(8-hydroxyquinolinyl-4-azo)phenylsulfanilamido-5,6-dimethoxypyrimidine, sulfadimethoxine, sulfadimidine, sulfamethoxazole, sulfamoxole, sulfadoxine, sulfaguanidine, sulfathiodimethoxine, sulfaquinoxaline, and p-(2-methyl-8-hydroxyquinolinyl-5-azo)-phenylsulfanilamido-5,6-dimethoxypyrimidine); and 2,4-diaminopyrimidines and salts thereof (eg. 2,4-diamino-6-ethyl-5-p-chlorophenylpyrimidine (Pyrimethamine), 2,4-diamino-5-(3',4',5'-trimethoxybenzyl)pyrimidine (Trimethoprim), 2,4-diamino-5-(3',4'-dimethoxybenzyl)pyrimidine

(Diaveridine), 2,4-diamino-5-(2'-isopropyl-4'-chlorophenoxy) pyrimidine, 2,4-diamino-5-methyl-6-sec-butyl-pyrido (2,3-d) pyrimidine, 2,4-diamino-5-methyl-6-benzylpyrido (2,3-d)pyrimidine, 2,4-diamino-6-benzylpyrido (2,3-d) pyrimidine, 2,4-diamino-5,6-trimethylenequinazoline, 2,4-diamino-5,6-tetramethylenequinazoline, 2,4-diamino-5-(4'-dimethylamino-3',5'-dimethoxybenzyl)pyrimidine 2,4-diamino-5-(2',4',5'-trimethoxybenzyl) pyrimidine, 2,4-diamino-5-(2'-ethyl-4',5'-dimethoxybenzyl)pyrimidine, and 2,4-diamino-5-(2'-methyl-4',5'-dimethoxybenzyl) pyrimidine (Ormetoprim), as well as the 2,4-diaminopyrimidine derivatives disclosed in European Patent No. 51879). A particularly preferred 2,4-diaminopyrimidine for use in pharmaceutical compositions according to the present invention is 2,4-diamino-5-(8-dimethylamino-7-methyl-5-quinolylmethyl)pyrimidine or a salt thereof. A particularly preferred sulphonamide is sulphadimidine or a salt thereof.

Preferred anthelmintics include levamisole, tetramisole, oxfendazole, mebendazole, fenbendazole, thiabendazole, albendazole and ivermectin.

Other biologically active substances which may be included in a composition according to the present invention include insecticides, larvicides, aquatic herbicides, and fish nutrients and vaccines, for release into rivers, reservoirs, lakes, ponds, pools, tanks and the like.

Water-swellaable polymers which may be utilised in the composition of the present invention include cellulose ethers, such as methylcellulose and hydroxypropylmethylcellulose (HPMC) such as are sold under the trade name 'Methocel'. Cellulose ethers which may be utilised in the present invention are generally those having a number average molecular weight in the range 10,000 to 150,000. Preferably the water swellaable polymer is hydroxypropylmethylcellulose, most preferably HPMC K15M, HPMC K100M and HPMC E4M.

The water swellable polymer is preferably present in the composition at a % weight concentration of between 0.1 to 5.0%, e.g. 0.1 to 4.0%, especially 0.5 to 2.5%.

Preferred compositions according to present invention are those comprising a biologically active substance, water swellable polymer material and optionally, one or more accessory ingredients, characterised in that the water swellable polymer material constitutes no more than 2% by weight of said composition.

As indicated hereinabove, applicants have found that decreasing the amount of polymer in the compositions according to the present invention can prolong the duration of release of the active ingredient. Thus, a sustained release formulation according to the present invention preferably contains no more than 1% by weight of polymer, for example between 0.1 and 1% by weight of polymer.

To achieve a particular release profile, eg. an immediate release followed immediately afterwards, or after an interval, by a slower prolonged release, it may be desirable to provide a mixture of two or more different formulations, which may for example be in the form of granules, each containing a different percentage of polymer.

Accessory ingredients which may be incorporated in a pharmaceutical composition according to the present invention are well known to those skilled in the art of human and veterinary pharmacy. Thus, accessory ingredients may include densification agents as described above; dense, water insoluble fillers (bulking agents) such as dibasic calcium phosphate, barium sulphate, or other fillers as described in US Patent Specification no 3, 773, 921; binders, such as polyvinylpyrrolidone, gelatin, casein, acacia, tragacanth, agar and pectin; and lubricants such as magnesium stearate, sodium stearate, calcium stearate, stearic acid, talc or silica. If desired the formulations may also contain pigments such as red or yellow iron oxide.

It will be appreciated that the type and amounts of accessory ingredients may be varied depending on the precise formulation required.

Densification agents will generally be present at concentrations of from 5 to 75% by weight of the total composition, preferably 15 to 50%. Fillers will generally comprise 0 to 95% of the total composition. Binding agents are preferably present in an amount ranging from 1 to 10% and lubricants in the range 0.1 to 2%.

Pharmaceutical dosage forms according to the present invention may be prepared by techniques known to those skilled in the art of human and veterinary pharmacy. Thus, for example they may be prepared by direct compression of the admixed ingredients. Alternatively, the ingredients may first be granulated and the granules compressed. When the dosage form is prepared by granulation it may be convenient to add a lubricant e.g. magnesium stearate after the granulation step. As will be understood by those skilled in the art, the degree of compression will affect the hardness of the dosage form. It is preferred that, when measured by the method described hereinafter, the hardness of dosage forms according to the present invention lies in the range 100 to 18000 Newtons, preferably 100 to 1000 N for a short-acting unit dose form and preferably 800 to 1800N for a long-acting unit dose form. It will be appreciated however that the optimum hardness and the degree of compression required for a given dosage form can readily be determined by routine tests.

It will be appreciated that whilst the amount of polymer present is a critical factor in determining the release rate of the active ingredient, the precise duration and pattern of release will be affected to some extent by other factors such as the nature of the active ingredient, the degree of compression used in manufacturing the dosage form and its overall size. In general a unit dosage form according to the present invention may provide release of the active ingredient for up to 10 days. Thus for example a short acting unit dose form may provide continuous release of the active ingredient over a period of 1 to 96 hours eg. 2 to 48 hours from the time of administration, and a long acting dosage form may release the active

ingredient during a period of 3 hours to 10 days eg. 12 hours to 7 days, from the time of administration.

In a preferred embodiment the present invention provides a short-acting veterinary bolus for oral administration to the rumen of an animal said bolus comprising one or more active ingredients, preferably an antibacterial agent such as 2,4-diamino-5-(8-dimethylamino-7-methyl-5-quinolylmethyl)pyrimidine or a salt thereof and/or a sulphonamide or a salt thereof, preferably sulphadimidine, together with a water swellable polymer, preferably hydroxypropylmethylcellulose, the polymer being at a % weight concentration of no more than 2%, preferably between 1 and 2%, and optionally one or more accessory ingredients such as a binder, lubricant, densification agent or pigment. In this embodiment the bolus typically contains from 1 to 8mg/kg of the pyrimidine, preferably approximately 4mg/kg; and from 9 to 72mg/kg of sulphadimidine, preferably approximately 36mg/kg. The unit dose form conveniently has a total weight of from 5 to 50g. The bolus preferably has a hardness (when measured by the method described hereinafter) of from 100 to 1000 Newtons, for example 140 to 180N for a 15g bolus and 300 to 900N for a 30g bolus. The length of the bolus is conveniently in the range 30 to 70mm preferably approximately 50mm, and its thickness is within the range 10 to 30mm, e.g. 12 to 13.5mm for a 15g bolus and 23 to 25mm for a 30g bolus.

In another preferred embodiment the present invention provides a long-acting veterinary bolus for administration to the rumen of an animal said bolus comprising one or more active ingredients, preferably an antibacterial agent such as 2,4-diamino-5-(8-dimethylamino-7-methyl-5-quinolylmethyl)pyrimidine or a salt thereof and/or a sulphonamide or a salt thereof, preferably sulphadimidine, together with a water swellable polymer, preferably hydroxypropylmethylcellulose, the polymer being at a % weight concentration of no more than 1%, preferably between 0.1 and 1%, and optionally one or more accessory ingredients such as a binder, lubricant, densification agent or pigment. In this embodiment the bolus typically contains from 6 to 16mg/kg of the pyrimidine, preferably approximately 8mg/kg; and from 54 to 144mg/kg of sulphadimidine, preferably approximately

72 mg/kg. The unit dose form conveniently has a total weight of from 5 to 50g. The bolus preferably has a hardness of from 800 to 1800 Newtons, for example 900 to 1500N for a 30g bolus. The length of the bolus is conveniently the range 30 to 70mm, preferably approximately 50mm, and its thickness is within the range 20 to 25mm, e.g. 21 to 23mm for a 30g bolus.

In a further aspect the present invention provides a pharmaceutical composition comprising a biologically active substance, water swellable polymer material and optionally, one or more accessory ingredients, characterised in that the water swellable polymer material constitutes no more than 7% by weight of the said composition, for use in the manufacture of a medicament.

The present invention also provides a method of treating a bacterial or helminthic infection which comprises the administration of a pharmaceutical composition, said composition comprising an antibacterial or anthelmintic agent, a water swellable polymer material which polymer constitutes no more than 7% by weight of the total composition, and optionally one or more accessory ingredients.

The present invention will now be illustrated by way of the following non-limiting examples. Compound A is 2,4-diamino-5-(8-dimethylamino-7-methoxy-5-quinolylmethyl)pyrimidine. Compound B is 2,4-diamino-5-(8-dimethylamino-7-methyl-5-quinolylmethyl)pyrimidine.

Examples

1. Compressed Granule Bolus (Short Acting)

<u>Ingredient</u>	<u>% Content by Weight</u>
Sulphadimidine	47.97
Compound A or Compound B	5.33
Iron Powder (325 Mesh)	29.20
Dibasic Calcium Phosphate	10.00
HPMC (Methocel K100M)	2.00
PVP K30	5.00
Magnesium stearate	0.50

All the ingredients apart from magnesium stearate were granulated. The magnesium stearate was added to the granulate and the mixture compressed using a Manesty 35T compressing machine to give boluses of the desired weight.

2. Compressed Granule Bolus (Long Acting)

<u>Ingredients</u>	<u>% Contents by Weight</u>
Sulphadimidine	47.97
Compound A or Compound B	5.33
Iron Powder (325 Mesh)	30.20
Dibasic Calcium Phosphate	10.00
HPMC (Methocel K100M)	1.00
PVP K30	5.00
Magnesium stearate	0.50

The ingredients were granulated and compressed together to form a bolus, as described in Example 1.

3. Compressed Granule Bolus (Mixed Formulation)

<u>Ingredients</u>	<u>Formulation I</u>	<u>Formulation II</u>
	<u>% Content Weight</u>	<u>% Content by Weight</u>
Sulphadimidine	47.97	47.97
Compound A or Compound B	5.33	5.33
Iron Powder (325 Mesh)	30.20	31.10
Dibasic Calcium Phosphate	10.00	10.00
HPMC (Methocel K100M)	1.00	0.10
PVP K30	5.00	5.00
Magnesium stearate	0.50	0.50

Formulations I and II were granulated and intimately mixed together in a 1:1 ratio then compressed together to form a bolus, as described in Example 1.

4. Compressed Granule Bolus (Long Acting)

<u>Ingredients</u>	<u>% Contents by Weight</u>
Sulphadimidine	47.97
Compound B	5.33
Iron Powder (325 Mesh)	28.2
Dibasic Calcium Phosphate	10.00
HPMC (Methocel K15M)	1.00
PVP K30	5.00
Magnesium stearate	0.50
Red iron oxide	2.00

The ingredients were granulated and compressed together to form a bolus as described in Example 1.

Examples 5A - 5F

The following formulations were prepared using sulphadimidine as active ingredient:-

	<u>% content by wt.</u>					
	5A	5B	5C	5D	5E	5F
Sulphadimidine	53.3	53.3	53.3	53.3	53.3	53.3
Iron Powder	30.95	30.7	30.45	30.2	30.2	30.2
Barium sulphate	10.0	10.0	10.0	10.0	10.0	10.0
HPMC (Methocel K15M)	0.25	0.5	0.75	1.0	-	-
HPMC (Methocel K100m)	-	-	-	-	1.0	-
HPMC (Methocel E4M)	-	-	-	-	-	1.0
PVP K 30*	5.0	5.0	5.0	5.0	5.0	5.0
Magnesium stearate	0.5	0.5	0.5	0.5	0.5	0.5

*2.5% w/w of PVP was added as a powder and 2.5% w/w as a solution having the following composition:-

	% w/w
PVP K30	23.8
Distilled water	38.1
Industrial methylated spirits	38.1

Method

All the ingredients apart from the magnesium stearate were granulated. The magnesium stearate was then added to the granulate and the mixture compressed using a Manesty 35T compressing machine, to give boluses of the desired weight.

Measurement of Hardness

The hardness of the unit dose forms prepared in accordance with the present invention was measured using a T30K Tensometer (J.J. Lloyd), which was modified so as to locate the dosage form in a 3-point pivot. The dosage form e.g. a bolus is supported on two lower pins which move in an upward direction until the dosage form meets an upper pin located midway between the two lower pins. Pressure is applied until the dosage form breaks and the force required to reach this point is recorded.

Serum profiles following oral administration to cattle

Example 6

Four cattle (nos 1-4) each received by oral administration a single 30g bolus formulated according to Example 1, containing 5.33% w/w of Compound B and 47.97% w/w of sulphadimidine (SDD). A further four cattle Nos. 5-8) each received by oral administration a single 30g bolus formulated according to Example 4, containing 5.33% w/w of Compound B and 47.97% w/w of SDD. Blood samples were taken from each animal at the time of dosing and at 3, 5, 7, 12, 24, 31, 48, 54, 72, 78, 96, 102, 120 and 168 hours after administration. The concentrations of compound B and SDD in the

serum were determined by bioassay and the Bratton-Marshall colorimetric method respectively.

The bodyweights of the cattle were as follows:

<u>Cattle No</u>	<u>Bodyweight (kg)</u>	<u>Cattle No</u>	<u>Bodyweight (kg)</u>
1	205	5	170
2	160	6	165
3	180	7	180
4	215	8	215

Results

Bolus of Example 1

<u>Time</u> <u>(hours)</u>	<u>Compound B $\mu\text{g}/\text{cm}^3$ serum</u>				<u>SDD $\mu\text{g}/\text{cm}^3$ serum</u>			
	<u>Animal No.</u>							
	<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>	<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>
0	0	0	0	0	0	0	0	0
3	0.07	0.05	0.06	0.05	23	23	23	21
5	0.14	0.12	0.13	0.11	50	44	40	39
7	0.27	0.23	0.23	0.19	65	64	59	50
12	0.43	0.49	0.47	0.46	72	89	78	63
24	0.75	0.98	0.85	0.68	38	68	44	37
27	1.60	1.80	1.80	1.10	28	53	38	27
31	1.40	1.30	1.40	0.82	21	36	30	19
48	0.57	0.62	0.63	0.49	2	8	7	3
54	0.43	0.43	0.50	0.37	0	5	3	2
72	0.18	0.22	0.23	0.16	0	1	1	1
78	0.13	0.13	0.18	0.13	0	0	0	0
96	0.05	0.06	0.10	0.05	0	0	0	0
102	0	0	0.06	0	0	0	0	0
120	0	0	0	0	0	0	0	0
168	0	0	0	0	0	0	0	0

Bolus of Example 4

<u>Time</u> (hours)	<u>Compound B $\mu\text{g}/\text{cm}^3$ serum</u>				<u>SDD $\mu\text{g}/\text{cm}^3$ serum</u>			
	<u>Animal No.</u>							
	<u>5</u>	<u>6</u>	<u>7</u>	<u>8</u>	<u>5</u>	<u>6</u>	<u>7</u>	<u>8</u>
0	0	0	0	0	0	0	0	0
3	0	0	0	0	1.5	2.5	2	2
5	0	0	0	0	2	5	4.5	4
7	0	0	0	0	3.5	7	7.5	9
12	0	0	0.06	0	6	9	12.5	9
24	0.17	0.15	0.22	0.14	11.5	16.5	24.5	16.5
27	0.27	0.24	0.41	0.23	11.5	14	24.5	15
31	0.27	0.26	0.54	0.32	12.5	15.5	23.5	16
48	0.37	0.30	0.67	0.46	11	12.5	28	12.5
54	0.32	0.29	0.67	0.36	12	12.5	19	14.5
72	0.37	0.25	0.67	0.38	9.5	11.5	19	11
78	0.29	0.26	0.60	0.36	10	9	10	10.5
96	0.29	0.21	0.35	0.39	6.5	8	1.5	7.5
102	0.24	0.20	0.26	0.35	6	8	1	7
120	0.22	0.17	0.14	0.21	5	7	1	5.5
168	0.13	0.10	0	0	4.5	5.5	0.5	1.5

Claims

1. A pharmaceutical composition for release of a biologically active substance into a desired environment, comprising said biologically active substance, water swellable polymer material and optionally, one or more accessory ingredients, characterised in that the water swellable polymer material constitutes no more than 7% by weight of the said composition.
2. A pharmaceutical composition according to claim 1, in unit dose form.
3. A pharmaceutical composition according to either of claims 1 or 2 for oral administration.
4. A pharmaceutical composition according to any of claims 1 to 3 for veterinary use.
5. A pharmaceutical composition according to claim 4 adapted for oral administration to the rumen of an animal.
6. A pharmaceutical composition according to claim 5 which is an intra-ruminal bolus provided with a means to inhibit regurgitation.
7. A pharmaceutical composition according to any of claims 1 to 6 wherein the lower weight limit of the water swellable polymer content is 0.01% by weight of the total composition.
8. A pharmaceutical composition according to any of claims 1 to 7 wherein the biologically active substance is an antibacterial or anthelmintic agent.
9. A pharmaceutical composition according to claim 8 wherein the antibacterial agent comprises a sulphonamide or a salt thereof and/or a 2,4-diaminopyrimidine or a salt thereof.

10. A pharmaceutical composition according to claim 9 wherein the antibacterial agent comprises 2,4-diamino-5-(8-dimethylamino-7-methyl-5-quinolylmethyl) pyrimidine or a salt thereof together with sulphadimidine or a salt thereof.
11. A pharmaceutical composition according to claim 10 which provides a dose of 2,4-diamino-5-(8-dimethylamino-7-methyl-5-quinolylmethyl) pyrimidine in the range 1 to 16 mg/kg and a dose of sulphadimidine in the range 9 to 144 mg/kg.
12. A composition according to claim 1 for use in the manufacture of a medicament.
13. A composition according to any of claims 8 to 11 for use in the treatment of bacterial or helminthic infections.

Claims AT - ES - GR

1. A method for the preparation of a pharmaceutical composition for release of a biologically active substance into a desired environment, which comprises bringing into association said biologically active substance, water swellable polymer material and optionally, one or more accessory ingredients, characterised in that the water swellable polymer material constitutes no more than 7% by weight of the said composition.
2. A method according to claim 1, wherein the pharmaceutical composition is in unit dose form.
3. A method according to either of claims 1 or 2 wherein the pharmaceutical composition is adapted for oral administration.
4. A method according to any of claims 1 to 3 wherein the pharmaceutical composition is adapted for veterinary use.
5. A method according to claim 4 wherein the pharmaceutical composition is adapted for oral administration to the rumen of an animal.
6. A method according to claim 5, wherein the pharmaceutical composition is an intra-ruminal bolus provided with a means to inhibit regurgitation.
7. A method according to any of claims 1 to 6 wherein the lower weight limit of the water swellable polymer content is 0.01% by weight of the total composition.
8. A method according to any of claims 1 to 7 wherein the biologically active substance is an antibacterial or anthelmintic agent.
9. A method according to claim 8 wherein the antibacterial agent comprises a sulphonamide or a salt thereof and/or a 2,4-diaminopyrimidine or a salt thereof.

10. A method according to claim 9 wherein the antibacterial agent comprises 2,4-diamino-5-(8-dimethylamino-7-methyl-5-quinolylmethyl) pyrimidine or a salt thereof together with sulphadimidine or a salt thereof.
11. A method according to claim 10 wherein the pharmaceutical composition provides a dose of 2,4-diamino-5-(8-dimethylamino-7-methyl-5-quinolylmethyl) pyrimidine in the range 1 to 16 mg/kg and a dose of sulphadimidine in the range 9 to 144 mg/kg.
12. A composition according to claim 1 for use in the manufacture of a medicament.
13. A composition according to any of claims 8 to 11 for use in the treatment of bacterial or helminthic infections.
14. A method for the treatment of bacterial infections in animals which comprises the administration of a composition as defined in any one of claims 8 to 11.